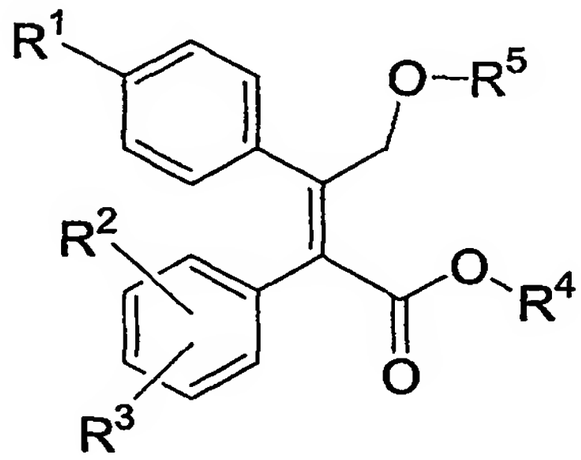
WHAT IS CLAIMED IS:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of:

(a) $S(O)_2CH_3$,
(b) $S(O)_2NH_2$,
(c) $S(O)_2NHC(O)CF_3$,
(d) $S(O)(NH)CH_3$,
(e) $S(O)(NH)NH_2$,
(f) $S(O)(NH)NHC(O)CF_3$,
(g) $P(O)(CH_3)OH$, and
(h) $P(O)(CH_3)NH_2$;

R^2 and R^3 each are independently selected from the group consisting of:

(a) hydrogen,
(b) halo,
(c) C_{1-6}alkoxy,
(d) C_{1-6}alkylthio,
(e) CN,
(f) CF_3,
(g) C_{1-6}alkyl, and
(h) N_3;

R^4 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl, optionally substituted with 1-3 substituents independently selected from the group consisting of:

(i) halo,

(ii) phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6,

(iii) $N(R^i)R^{ii}$, wherein R^i and R^{ii} are each independently selected from the group consisting of hydrogen and C_{1-4}alkyl,

(iv) $-CO_2R^{iii}$, wherein R^{iii} is hydrogen or C_{1-4}alkyl,

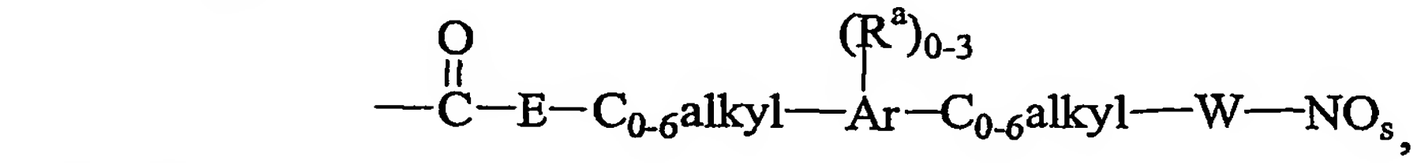
(c) phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^5 is selected from the group consisting of:

(a) $-NO_s$,

(b) $-C(O)-E-C_{1-10}alkyl-W-NO_s$,

(c)



wherein:

each s is independently 1 or 2,

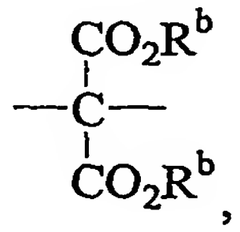
E is a bond, oxygen, sulfur or –C(O)-O-,

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)



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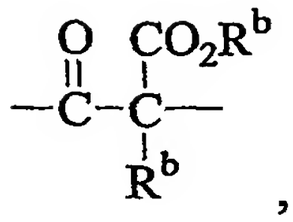


,

Ar is selected from the group consisting of: phenyl, naphthyl and HET^3,

each R^a is independently selected from the group consisting of:

(1) halo,
(2) C_{1-6}alkyl,
(3) C_{1-6}alkoxy,
(4) C_{1-6}alkylthio,
(5) OH,
(6) CN,
(7) CF_3,
(8) CO_2R^7, and
(9) C_{0-6}alkyl-W-NO_S;

each Rb is independently selected from the group consisting of:

(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

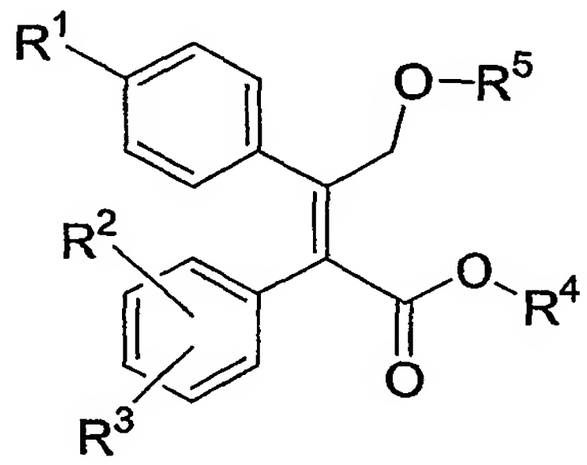
R^6, R^7 and R^8 are each independently selected from the group consisting of

(a) hydrogen,
(b) C_{1-6}alkyl; and

HET^1, HET^2, HET^3, HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl,

indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

2. A compound according to Claim 1 of Formula I



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of:

(a) $S(O)_2CH_3$,

(b) $S(O)_2NH_2$,

(c) $S(O)_2NHC(O)CF_3$,

(d) $S(O)(NH)CH_3$,

(e) $S(O)(NH)NH_2$,

(f) $S(O)(NH)NHC(O)CF_3$,

(g) $P(O)(CH_3)OH$, and

(h) $P(O)(CH_3)NH_2$;

R^2 and R^3 each are independently selected from the group consisting of:

(a) hydrogen,

(b) halo,

(c) C_{1-6}alkoxy,

(d) C_{1-6}alkylthio,

(e) CN,

(f) CF_3,

(g) C_{1-6}alkyl, and

(h) N_3;

R^4 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

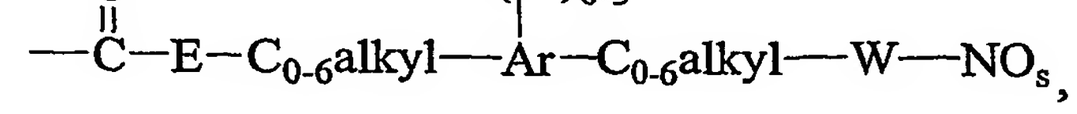
(c) phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^5 is selected from the group consisting of:

(a) $-NO_s$,

(b) $-C(O)-E-C_{1-10}alkyl-W-NO_s$,

(c)



wherein:

each s is independently 1 or 2,

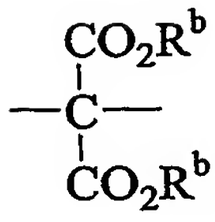
E is a bond, oxygen, sulfur or –C(O)-O-,

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)



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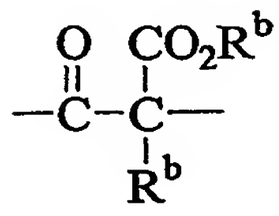


Ar is selected from the group consisting of: phenyl, naphthyl and HET^3,

each R^a is independently selected from the group consisting of:

(1) halo,
(2) C_{1-6}alkyl,
(3) C_{1-6}alkoxy,
(4) C_{1-6}alkylthio,
(5) OH,
(6) CN,
(7) CF_3,
(8) CO_2R^7, and
(9) C_{0-6}alkyl-W-NO_S;

each Rb is independently selected from the group consisting of:

(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

R^6, R^7 and R^8 are each independently selected from the group consisting of

(a) hydrogen,
(b) C_{1-6}alkyl; and

HET^1, HET^2, HET^3, HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

3. The compound according to Claim 2 wherein

R^1 is $S(O)_2CH_3$, and

R^2 and R^3 are both hydrogen.

4. The compound according to Claim 3 wherein:

R^4 is C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^6 is selected from the group consisting of

(a) hydrogen,
(b) C_{1-6}alkyl; and

HET^1 is selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

5. The compound according to Claim 4 wherein R^4 is methyl, ethyl, propyl or isopropyl.

6. The compound according to Claim 3 wherein:

R^4 is phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^6 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl; and

HET^2 is selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl,

isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

7. The compound according to Claim 3 wherein R^5 is $-NO_s$, wherein s is 1 or 2.

8. The compound according to Claim 3 wherein R^5 is -C(O)-E-C_{1-10}alkyl-W-NO_s, wherein:

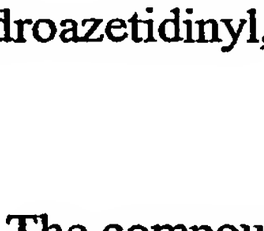
s is 1 or 2,

E is a bond, oxygen, sulfur or –C(O)-O-,
W is selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)



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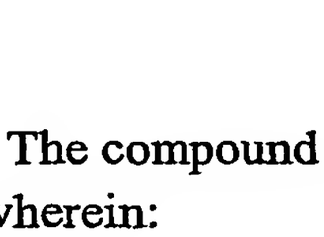


each R^b is independently selected from the group consisting of:

(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

R^8 is selected from the group consisting of

(a) hydrogen and

(b) C_{1-6}alkyl; and

HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

9. The compound according to Claim 8 wherein:

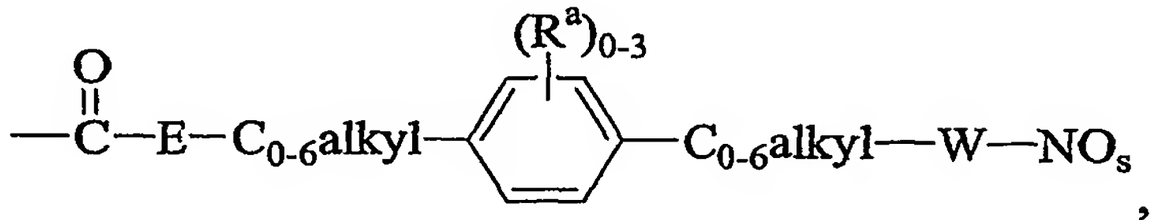
E is a bond or oxygen;

s is 2;

W is oxygen; and

R^4 is hydrogen, methyl, ethyl, propyl or isopropyl.

10. The compound according to Claim 3 wherein R^5 is



wherein:

each s independently 1 or 2,

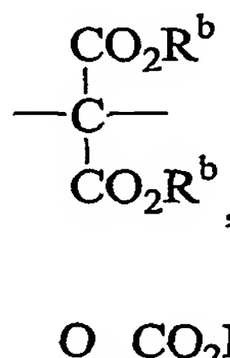
E is a bond, oxygen, sulfur or –C(O)-O-,

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)



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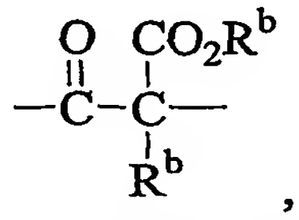

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each R^a is independently selected from the group consisting of:

(1) halo,

(2) C_{1-6}alkyl,

(3) C_{1-6}alkoxy,

(4) C_{1-6}alkylthio,

(5) OH,
(6) CN,
(7) CF_3,
(8) CO_2R^7, and
(9) C_{0-6}alkyl-W-NO_S;

each Rb is independently selected from the group consisting of:
(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

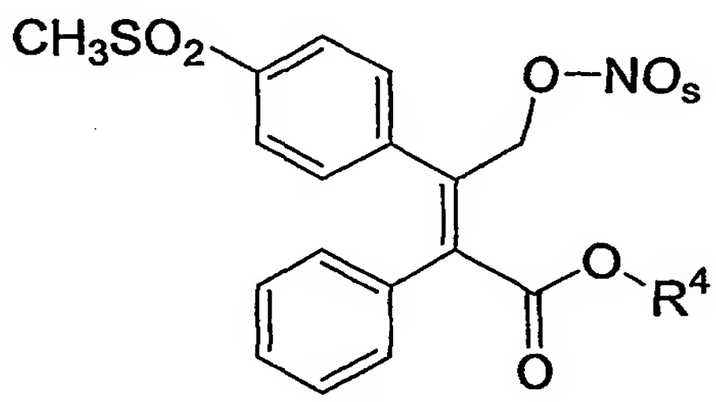
(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

R^7 and R^8 is selected from the group consisting of
(a) hydrogen and
(b) C_{1-6}alkyl; and

HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl,

dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

11. A compound according to Claim 2 of Formula II



II

or a pharmaceutically acceptable salt thereof, wherein

R^4 is selected from the group consisting of:

(a) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

(b) phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^6 is selected from the group consisting of

(a) hydrogen and

(b) C_{1-6}alkyl;

s is 1 or 2; and

HET^1 and HET^2 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl,

benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

12. The compound according to Claim 11 wherein R^4 is methyl, ethyl, propyl or isopropyl.

13. The compound according to Claim 11 wherein

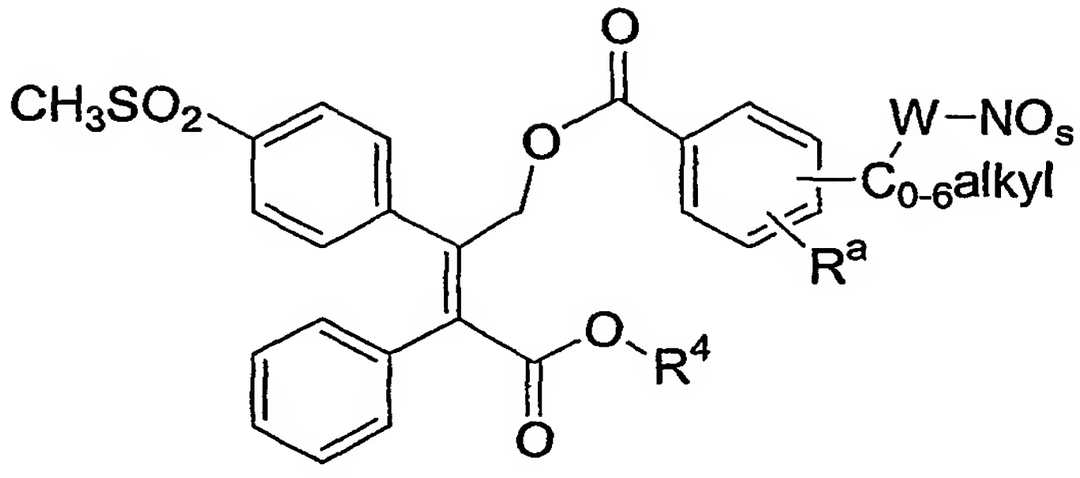
R^4 is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6; and

R^6 is selected from the group consisting of

(a) hydrogen and
(b) C_{1-6}alkyl.

14. The compound according to Claim 11 wherein s is 2.

15. A compound according to Claim 2 of Formula III



III

or a pharmaceutically acceptable salt thereof, wherein

R^4 is selected from the group consisting of:

(a) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

(b) phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^6 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl;

R^a is hydrogen or C_{0-6}alkyl-W-NO_s.

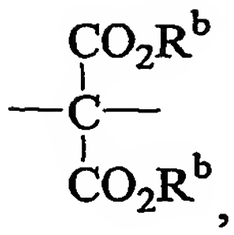
each s is independently 1 or 2,

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)



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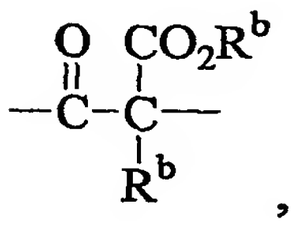


each Rb is independently selected from the group consisting of:

(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

R^8 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl; and

HET^1, HET^2, HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl,

dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

16. The compound according to Claim 15 wherein R^4 is methyl, ethyl, propyl or isopropyl.

17. The compound according to Claim 15 wherein

R^4 is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6; and

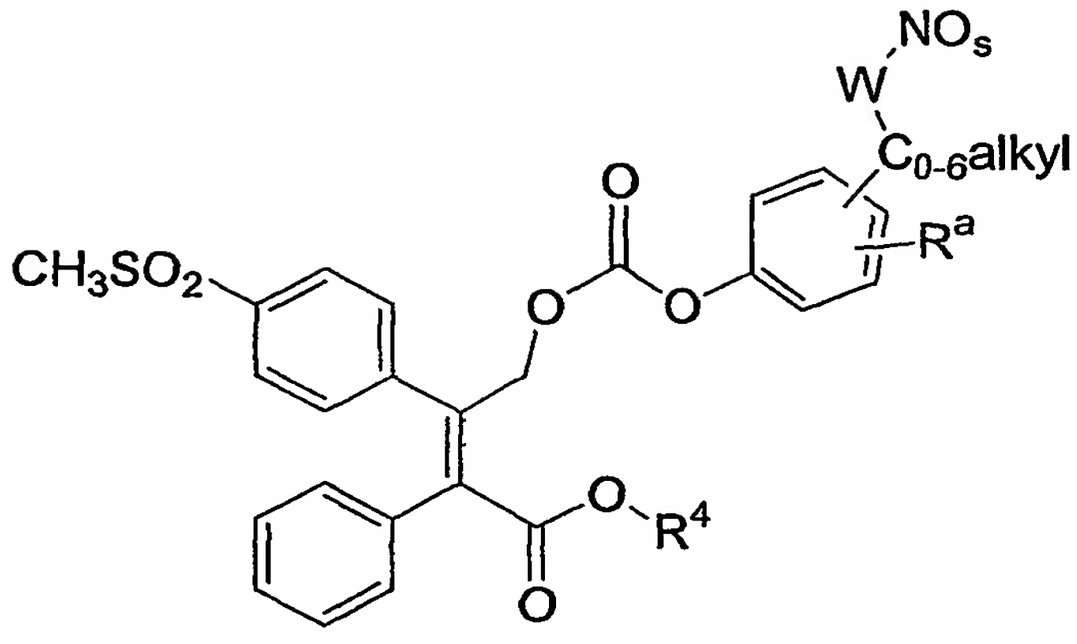
R^6 is selected from the group consisting of

(a) hydrogen and
(b) C_{1-6}alkyl.

18. The compound according to Claim 15 wherein s is 2 and W is oxygen.

19. The compound according to Claim 15 wherein R^a is $-CH_2$-W-NO_s.

20. A compound according to Claim 2 of Formula IV



IV

or a pharmaceutically acceptable salt thereof, wherein

R^4 is selected from the group consisting of:

(a) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

(b) phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^6 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl;

R^a is hydrogen or C_{0-6}alkyl-W-NO_s.

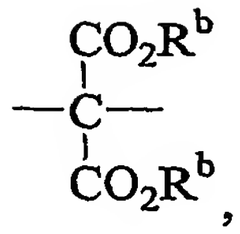
each s is independently 1 or 2;

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)



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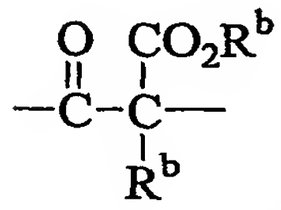
(4)



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each Rb is independently selected from the group consisting of:

(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

R^8 is selected from the group consisting of

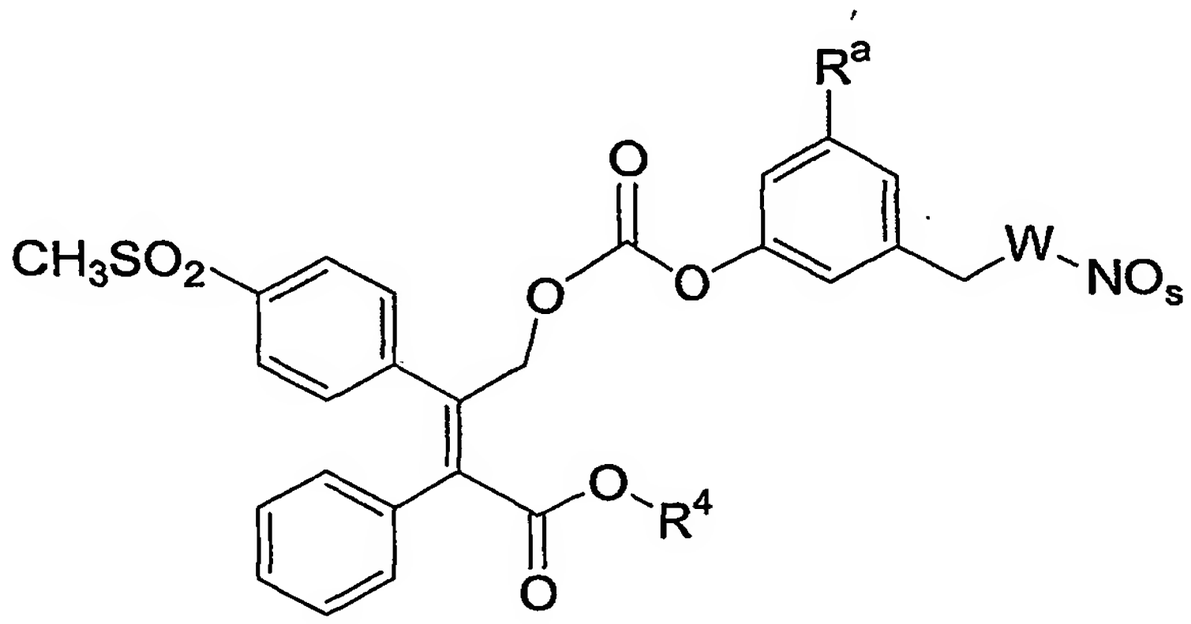
(a) hydrogen,

(b) C_{1-6}alkyl; and

HET^1, HET^2, HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl,

dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

21. The compound according to Claim 20 of Formula IVa



IVa

or a pharmaceutically acceptable salt thereof, wherein

R^4 is selected from the group consisting of:

(a) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^1, each of said phenyl, naphthyl or HET^1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

(b) phenyl, naphthyl or HET^2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6;

R^6 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl;

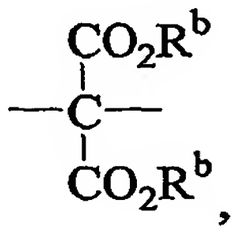
R^a is hydrogen or C_{0-6}alkyl-W-NO_s.

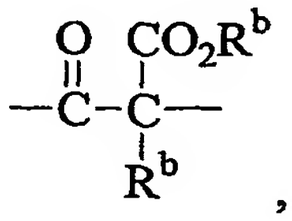
each s is independently 1 or 2;

each W is independently selected from the group consisting of:

(1) oxygen,

(2) sulfur,

(3)  ,

(4)  ,

each Rb is independently selected from the group consisting of:

(1) C_{1-6}alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET^4, each of said phenyl, naphthyl or HET^4 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8; and

(2) phenyl, naphthyl or HET^5, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^8;

R^8 is selected from the group consisting of

(a) hydrogen,

(b) C_{1-6}alkyl; and

HET^1, HET^2, HET^4 and HET^5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl,

pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

22. The compound according to Claim 21 wherein R^4 is methyl, ethyl, propyl or isopropyl.

23. The compound according to Claim 21 wherein

R^4 is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, OH, CN, CF_3, and CO_2R^6; and

R^6 is selected from the group consisting of

(a) hydrogen and

(b) C_{1-6}alkyl.

24. The compound according to Claim 21 wherein s is 2 and W is oxygen.

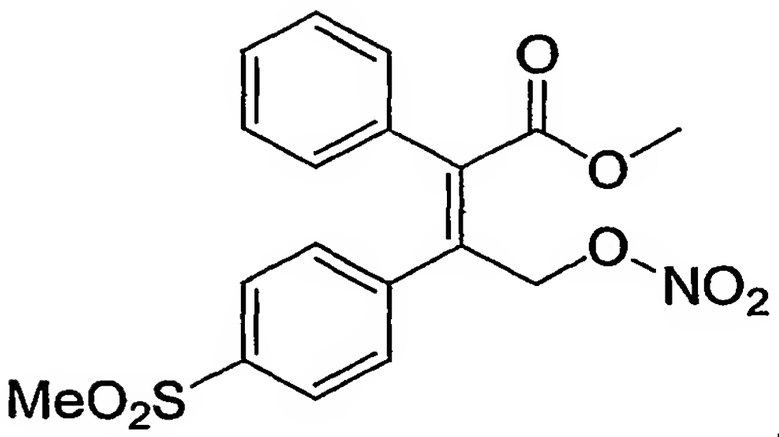
25. The compound according to Claim 21 wherein R^a is $-CH_2\text{-}W\text{-}NO_s$.

26. The compound according to Claim 1 wherein: R^4 is C_{1-6}alkyl, mono-substituted with

(i) $N(R^i)R^{ii}$, wherein R^i and R^{ii} are each independently selected from the group consisting of hydrogen and C_{1-4}alkyl or

(ii) $-CO_2R^{iii}$, wherein R^{iii} is hydrogen or C_{1-4}alkyl.

27. A compound selected from the following group:



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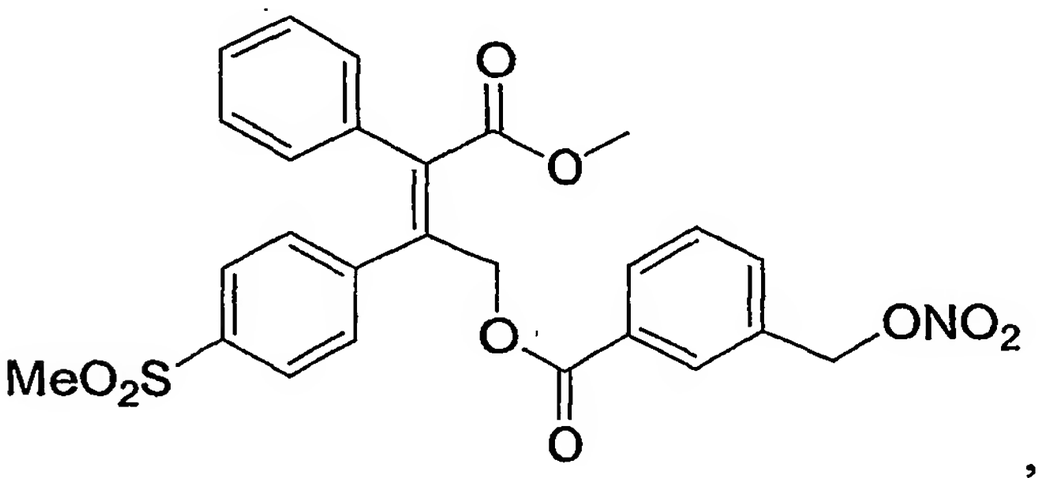

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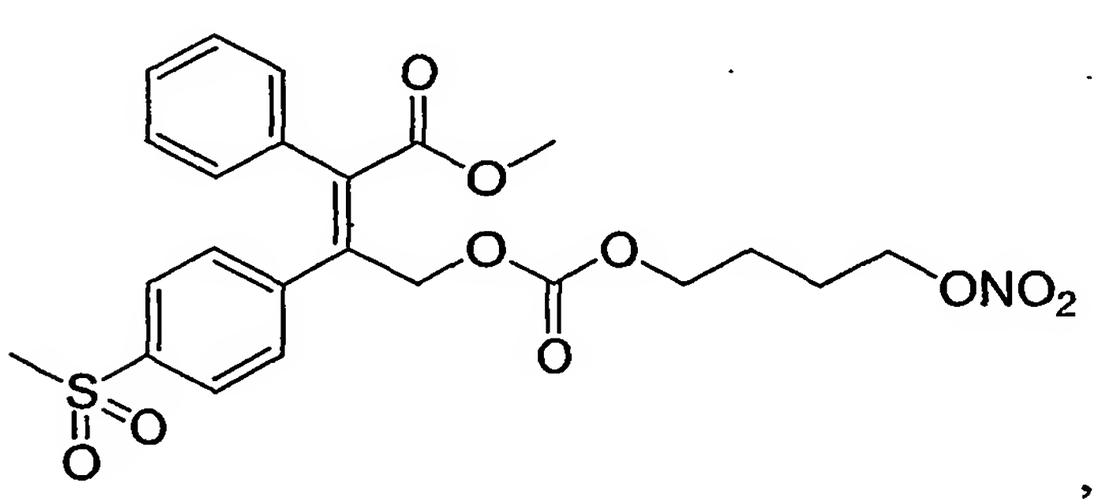

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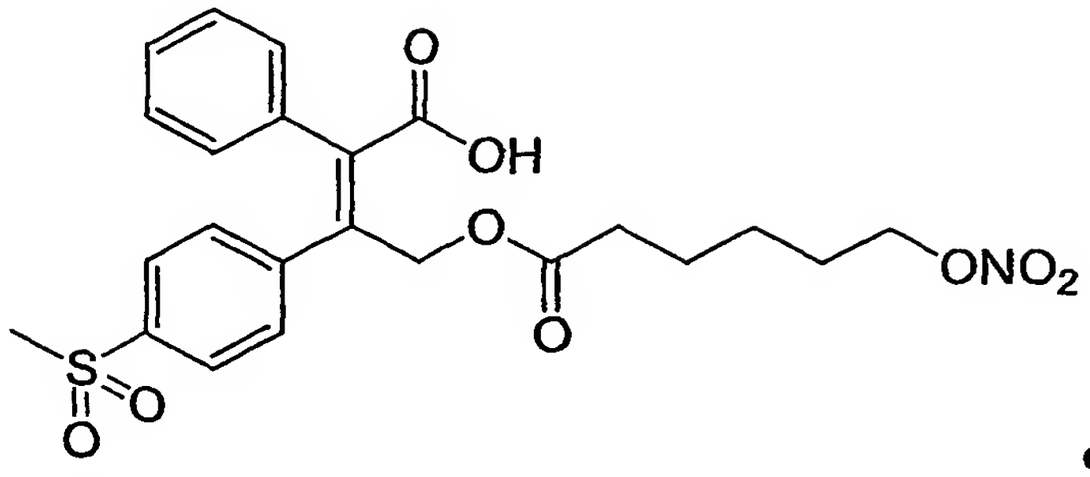
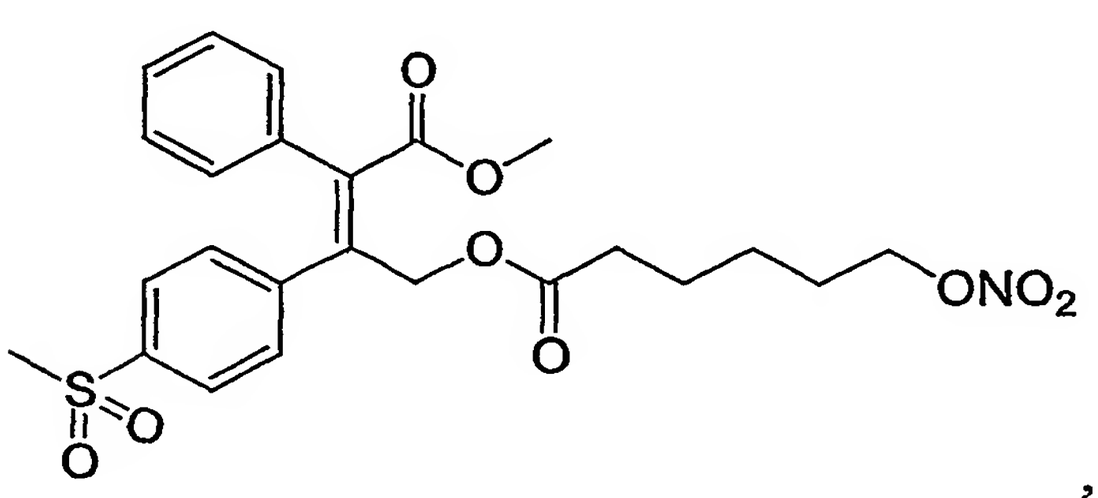


or a pharmaceutically acceptable salt thereof,



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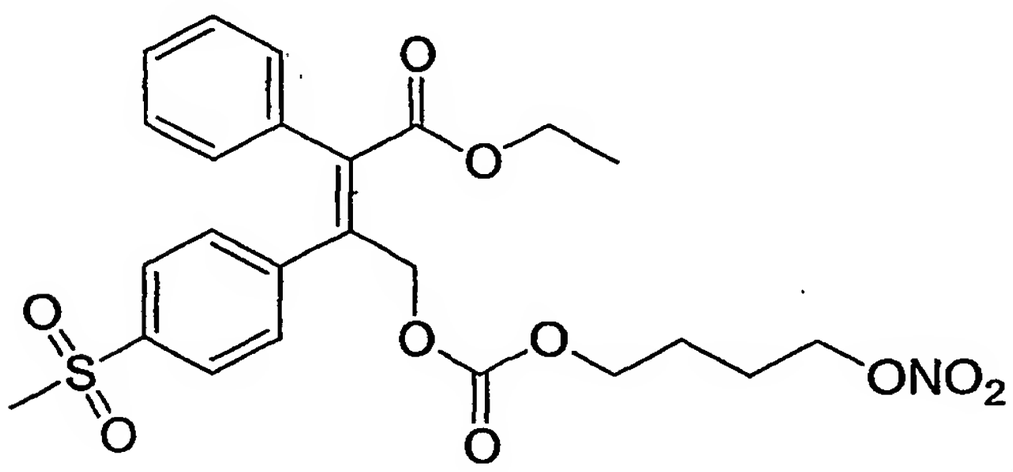

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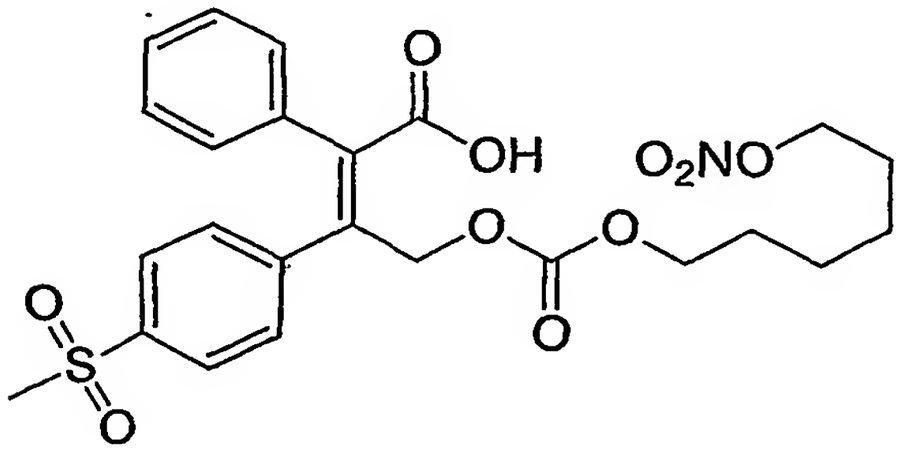
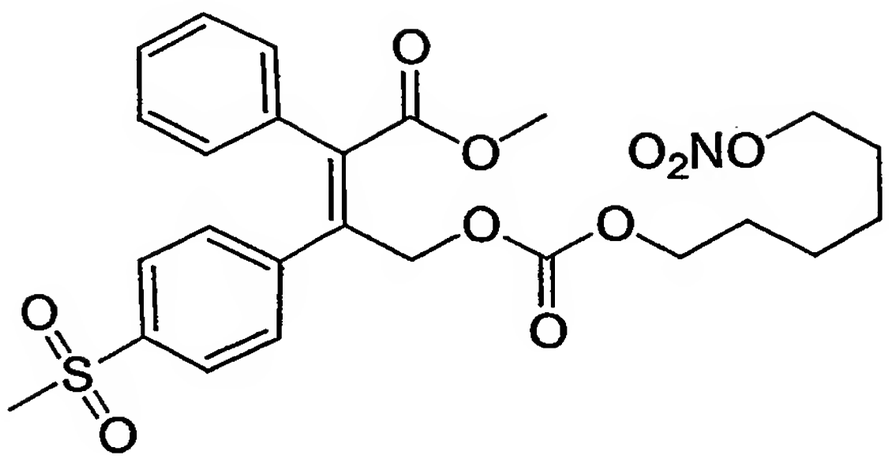


or a pharmaceutically acceptable salt thereof,



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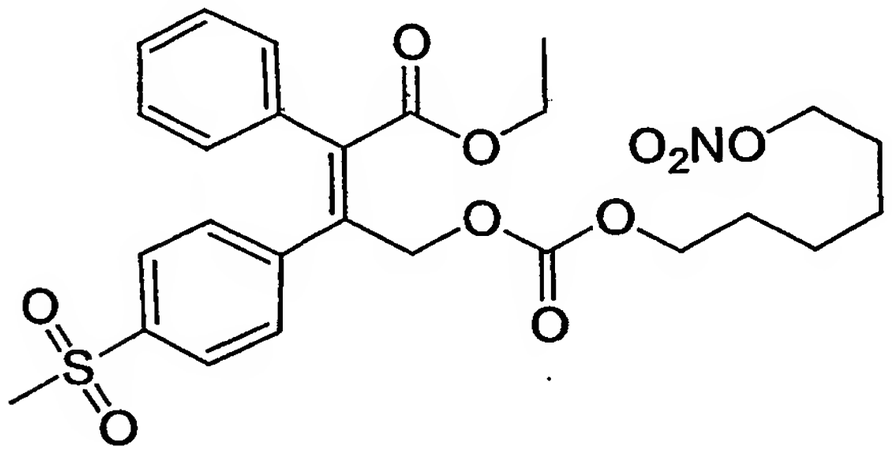

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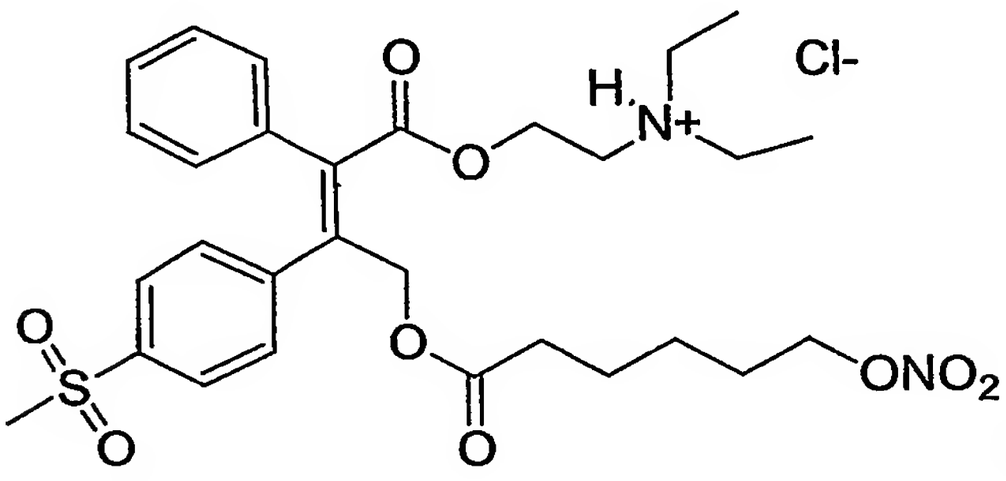
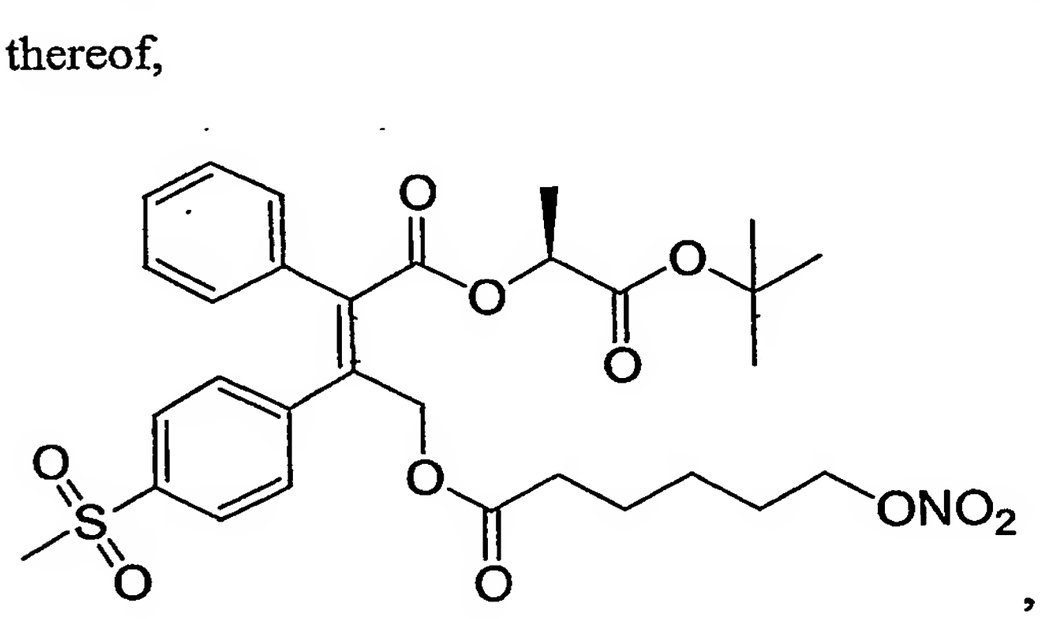


or a pharmaceutically acceptable salt thereof,



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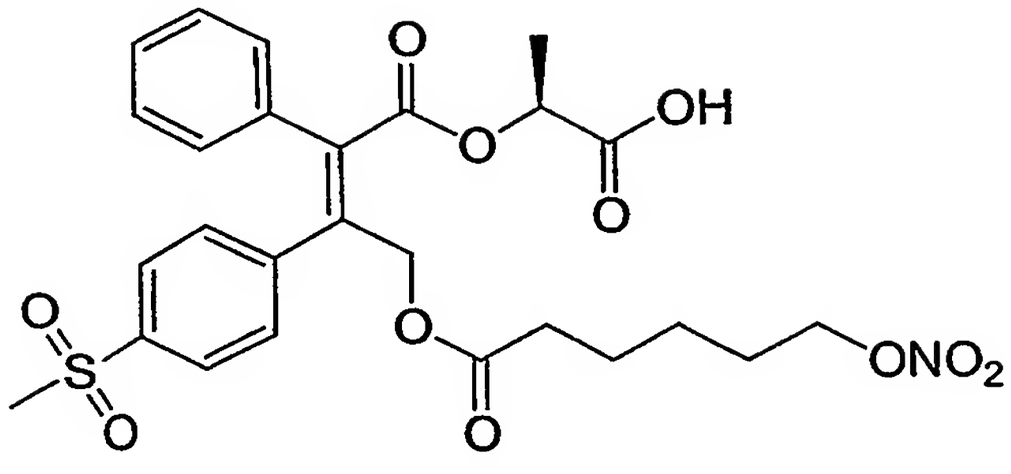
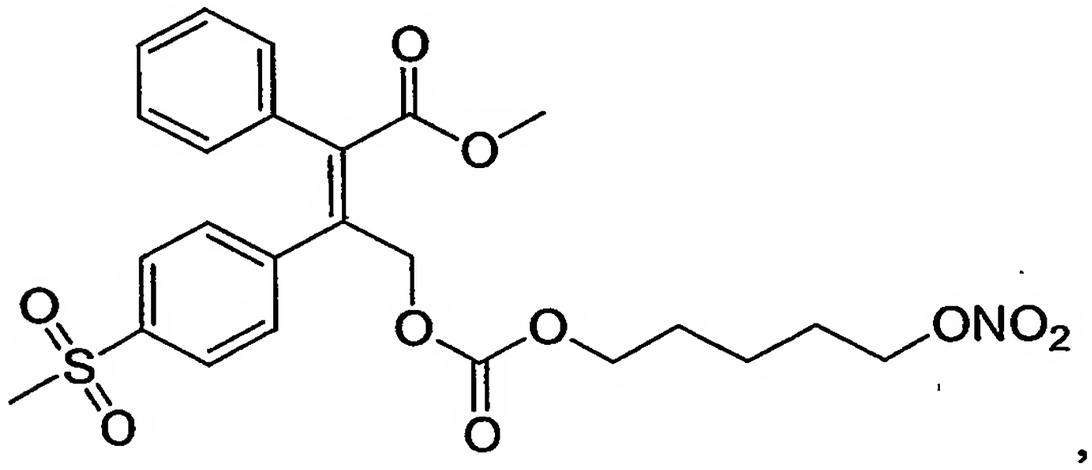


or a pharmaceutically acceptable salt thereof,



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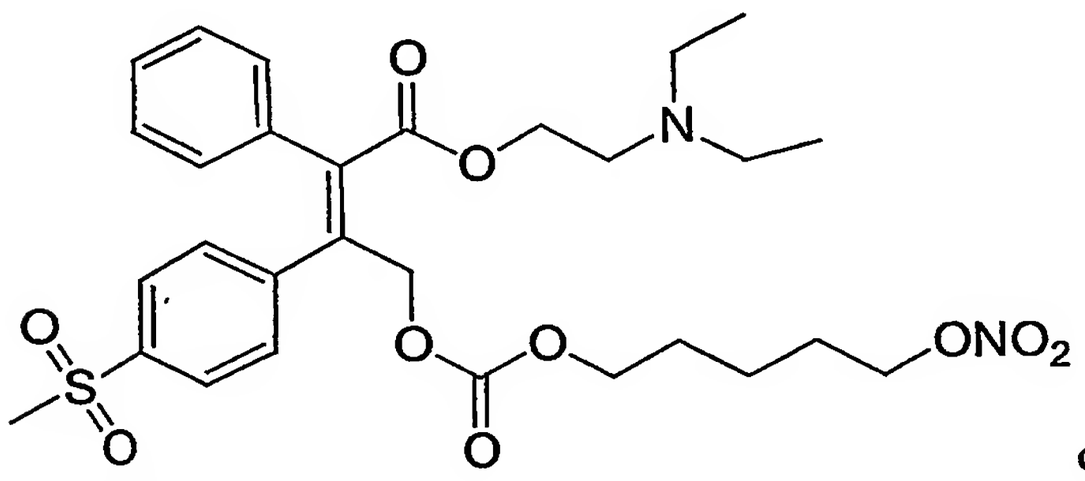
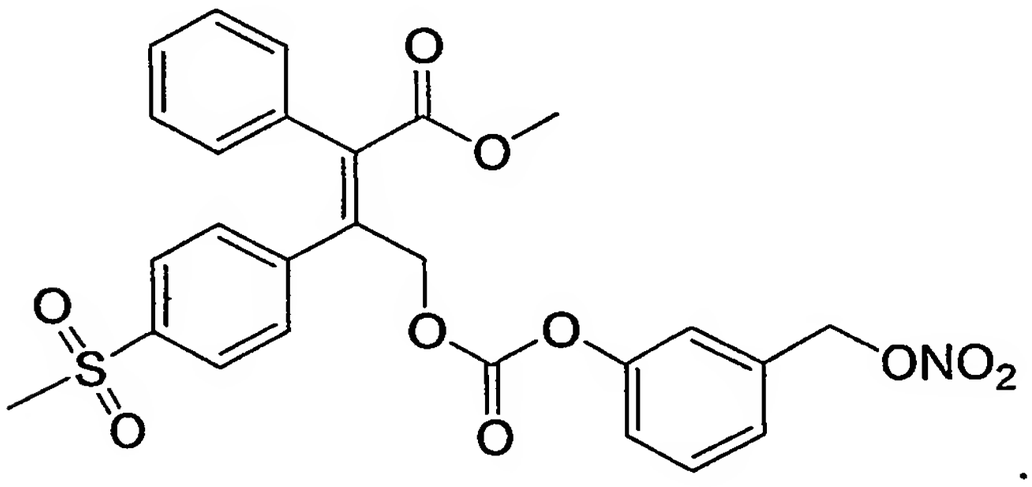


or a pharmaceutically acceptable salt thereof, and



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28. A method of treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to Claim 1.

29. The method according to Claim 28 wherein the patient is also at risk of a thrombotic cardiovascular event.

30. A method of treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preference to COX-1 comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to Claim 1.

31. The method according to Claim 30 wherein the patient is also at risk of a thrombotic cardiovascular event.

32. A method for treating a chronic cyclooxygenase-2 mediated disease or condition and reducing the risk of a thrombotic cardiovascular event in a human patient in need of such treatment and at risk of a thrombotic cardiovascular event comprising orally concomitantly or sequentially administering to said patient a compound according to Claim 1 in an amount effective to treat the cyclooxygenase-2 mediated disease or condition and aspirin in an amount effective to reduce the risk of the thrombotic cardiovascular event.

33. The method according to Claim 32 wherein the compound is administered orally on a once daily basis.

34. The method according to Claim 32 wherein the compound is administered orally on a twice daily basis.

35. The method according to Claim 32 wherein the cyclooxygenase-2 selective mediated disease or condition is selected from the group consisting of: osteoarthritis, rheumatoid arthritis and chronic pain.

36. The method according to Claim 32 wherein aspirin is administered at a dose of about 30 mg to about 1 g.

37. The method according to Claim 36 wherein aspirin is administered at a dose of about 80 to about 650 mg.

38. The method according to Claim 37 wherein aspirin is administered at a dose of about 81 mg or about 325 mg.

39. The method according to Claim 32 wherein aspirin is orally administered once daily.

40. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, and aspirin in combination with a pharmaceutically acceptable carrier.

41. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

42. A compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in medical therapy.

43. A compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent.

44. Use of a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for treating cyclooxygenase mediated diseases advantageously treated by selective inhibition of COX-2 in preference to COX-1